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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/520,436	KINGSLAND ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11 and 16-27* is/are pending in the application.

4a) Of the above claim(s) *16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/28/06; 11/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-7, 11 and 16-27 are pending.

2. Applicant's election of Group I (now claims 1-7, 11 and 24-27) in the reply filed on October 30, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The request for rejoinder of Group III, drawn to lyophilized fibrinogen which is ultimately dependent on the elected method (claims 11, 1, 3 and 7) is acknowledged.

However, it is noted that the method of claims 1, 3, 7 and 11 do not recite a method of making a lyophilized fibrinogen. The method of group I merely drawn to a method for separation and purification of fibrinogen and at least one other protein such as plasminogen and/or factor XIII. Therefore, the product as claimed, which can be made and/or isolate by a different process, will not ultimately dependent from the claimed method will not be rejoined at this time.

3. Claims 16-23 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-7, 11 and 24-27, drawn to a method for separation and purification of fibrinogen and at least one other protein and fibrinogen prepared by said process, Fibrinogen prepared by said process, are being acted upon in this Office Action.

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 1-7, 11 and 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: the buffer condition and pH that selectively eluting the fibrinogen off which one or more immobilized metal ion affinity chromatography matrix, i.e., copper, zinc metal ion affinity chromatography matrix are missing in the claims, see specification, paragraph bridging pages 17 and 18.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,169,936 (issued Dec 8, 1992; PTO 1449).

The '936 patent teaches a method for separation and purification of human fibrinogen and at least one other protein such as impurity which comprises the steps of: loading or contacting a solution comprising human fibrinogen and at least one other protein such as contaminants such as lysine onto an immobilized metal ion affinity chromatography matrix such as copper (II), nickel (II) or zinc (II) (see claims 1 and 15-17 of the '936 patent, col. 5, line 24-48, col. 10, lines 21-52, in particular), and selectively eluting the fibrinogen and the at least one other protein separately from the matrix (see claim 16 step b, in particular). Thus, the reference teachings anticipate the claimed invention.

10. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Hari et al (J Biomed Mater Res 50: 110-113, 2000; PTO 892).

Hari et al teach a method for separation and purification of fibrinogen and at least one other protein such as human IgG, albumin which comprises the steps of: loading a solution comprising albumin, γ-globulin, fibrinogen, and IgG onto to an immobilized metal ion affinity chromatography matrix such as copper metal ions immobilized onto cellulose membrane matrix under condition such that all proteins bind to the matrix (see page 110, col. 2, page 111, col. 1, first full paragraph, and paragraph bridging col. 1 and 2, page 112, Table I, in particular) and selectively eluting the fibrinogen and the at least one other protein separately from the matrix

within 5 hours (see page 111, col. 2, first paragraph, in particular). Hari et al teach copper is a group-specific ligand, it could be immobilized onto hollow fiber cellulose cartridges, its simplicity, and low cost, could be used as an inexpensive affinity membrane immunoadsorbent (see page 110, col. 2, page 113, in particular). Thus, the reference teachings anticipate the claimed invention.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-7, 11 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/25748 (published Sept 1995; PTO 1449) in view of Hari et al (J Biomed Mater Res 50: 110-113, 2000; PTO 1449) and Chaga et al (J Biochem Biophys Methods 49: 313-334, 2001; PTO 892).

The WO 95/25748 publication teaches a method for co-purification of fibrinogen and factor XIII which comprises the steps of loading a solution comprising fibrinogen, factor XIII and plasminogen onto cation affinity column such as lysine affinity column or lysine Sepharose 4B under conditions such that the plasminogen is removed by adsorbing to the lysine sepharose column (see entire document, page 8, line 9-20, claims 1, in particular). The publication teaches the removal of plasminogen is important because when converted to plasmin, it will break down fibrinogen and fibrin molecules. The latter are formed from interaction between fibrinogen and thrombin in the fibrin sealant to be produced from the composition (see page 8, line 18-22, in

particular). The publication further teaches concentrating the fibrinogen by ultrafiltration to a desired concentration such as 20 mg/ml or less before the step of lyophilized the composition (see page 12, line 20, page 35, line 1, page 18, line 1-5, page 18, line 21-22, in particular). The reference 20 mg/ml or less would include the claimed term of approximately 15 to 30 mg/ml such as 14, 15, 16, 17, 18, 19, and 20 mg/ml. The WO 95/25748 publication further teaches combining the fibrinogen with any suitable stabilizer such as human albumin, and/or a detergent such as polysobate-80 (see page 17, line 26-30, in particular). The reference solution comprising fibrinogen and factor XIII is from a fibrinogen containing plasma fraction such as pooled blood fraction (see page 5, second paragraph, in particular). The reference fibrinogen and factor XIII are coeluted from the column since plasminogen is removed from the column by adsorbing to the lysine sepharose column (see entire document, page 8, line 9-20, claims 1, in particular). The term "comprises" is open-ended. It expands the claimed method to include additional steps. Claim 4 is included in this rejection because it is within the purview of one of ordinary skill in the purification art to elute the bound plasminogen separately to regenerate the column. Claims 2-3 are included in this rejection because the term "comprising" is open-ended. It expands the solution to include additional protein such as plasminogen, and factor XIII.

The invention differs from the teachings of the reference only in that the method for co-purification of fibrinogen and factor XIII wherein the column is metal ion affinity column instead of lysine affinity column and selectively eluting the fibrinogen and the factor XIII from the matrix.

Hari et al teach a method for separation and purification of fibrinogen and at least one other protein such as human IgG, albumin which comprises the steps of: loading a solution comprising albumin, γ-globulin, fibrinogen, and IgG onto to an immobilized metal ion affinity chromatography matrix such as copper metal ions immobilized onto cellulose membrane matrix under condition such that all proteins bind to the matrix (see page 110, col. 2, page 111, col. 1, first full paragraph, and paragraph bridging col. 1 and 2, page 112, Table I, in particular) and then selectively eluting the fibrinogen and the at least one other protein separately from the matrix within 5 hours (see page 111, col. 2, first paragraph, in particular). Hari et al teach copper is a group-specific ligand, it could be immobilized onto hollow fiber cellulose cartridges, its simplicity, and low cost, could be used as an inexpensive affinity membrane immunoadsorbent (see page 110, col. 2, page 113, in particular).

Chaga et al teach immobilized metal ion affinity chromatography (IMAC), at present, is one of the most popular methods for purification of recombinant proteins due to its versatility, high capacity, high recovery, mild loading, mild elution, complete regeneration of column and low cost (see page 314, Table 1, in particular). IMAC has been extensively use in the successful purification of protein from complex biological samples (see page 315, last paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute cation column such as lysine affinity column in the method of separation and purification of fibrinogen of the WO 95/25748 publication for the immobilized metal ion affinity chromatography matrix for separation of fibrinogen from other proteins as taught by Hari et al since IMAC is most popular methods for purification as taught by Chaga et al.

One having ordinary skill in the art would have been motivated to substitute the lysine affinity column for the immobilized metal ion affinity column in affinity chromatography (IMAC) because of IMAC's versatility, high capacity, high recovery, mild loading, mild elution, complete regeneration of column and low cost (see page 314, Table 1, in particular). IMAC has been extensively use in the successful purification of protein from complex biological samples as taught by Chaga et al (see page 315, last paragraph, in particular). One having ordinary skill in the art would have been motivated with the expectation of success to use immobilized metal ion affinity column because Hari et al has demonstrated that fibrinogen binds to the copper metal ions immobilized onto cellulose membrane matrix (see page 110, col. 2, page 111, col. 1, first full paragraph, and paragraph bridging col. 1 and 2, page 112, Table I, in particular).

One having ordinary skill in the art would have been motivated to purify fibrinogen without the plasminogen because the WO 95/25748 publication teaches removal of plasminogen is important because when converted to plasmin, it will break down fibrinogen and fibrin molecules and factor XIII is important for the formation of stable fibrin sealant to be produced from the composition (see page 8, line 18-22, in particular).

14. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/25748 publication (published Sept 1995; PTO 1449) in view of Hari et al (J Biomed Mater Res 50: 110-113, 2000; PTO 1449) and Chaga et al (J Biochem Biophys Methods 49: 313-334, 2001; PTO 892) as applied to claims 1-7, 11 and 24-26 mentioned above and further in view of WO 96/17631 publication (published June 1996; PTO 1449).

The combined teachings of the WO 95/25748 publication, Hari et al and Chaga et al have been discussed supra.

The invention in claim 27 differs from the teachings of the references only in that the method for co-purification of fibrinogen and factor XIII further comprising the step of subjecting the lyophilized fibrinogen formulation to dry heat treatment.

The WO 96/17631 publication teaches lyophilized fibrinogen is heat treated such as at 70 °C to 100°C for up to 96 hours and such heat treatment is more effective in viral inactivation (see page 8, lines 6 through page 10, line 4, page 14, second paragraph, claims 18-19 of the publication, page 18, second full paragraph, in particular). WO 96/17631 publication teaches various stabilizers such as sucrose (carbohydrate) and arginine (amino acid) to protect the formulation during freezing and to stabilize during subsequent heat treatment (see page 13, third paragraph, in particular). The WO 96/17631 publication teaches the presence of factor XIII is important where the lyophilized fibrinogen is to be used to produce fibrin sealant (see page 8, line 6-10, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the step of heat treatment after lyophilization as taught by WO 96/17631 publication for the method of co-purification of fibrinogen and factor XIII using immobilized metal ion affinity chromatography matrix as taught by the WO 95/25748 publication and Hari et al.

One having ordinary skill in the art would have been motivated to do this because the WO 96/17631 publication teaches the advantage of heat treatment after lyophilization is that it is more effective in viral inactivation (see page 8, lines 6 through page 10, line 4, page 14, second paragraph, claims 18-19 of the publication, page 18, second full paragraph, in particular). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

17. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
December 5, 2008